Molecular Dynamics Simulations of Peptide Nucleic Acid at Lipid Bilayer

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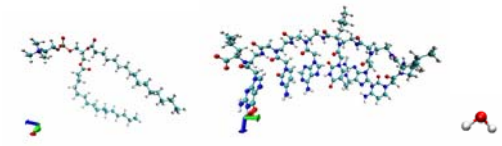
Lipids are relatively water-insoluble or nonpolar compounds of biological origin. The simplest lipids are linear fatty acids molecules. Most of lipids' molecules have some polar or hydrophilic ("water-loving") part in addition to being largely nonpolar or hydrophobic ("water-fearing"). This amphiphilic character of the molecules makes them a key building block of cell membranes, because in water the heads of lipids tend to face the polar, aqueous environment, while the hydrophobic tails tend to contact one another and minimize the contact with the water molecules. As a final effect of the opposite tendencies, lipid molecules spontaneously form clusters, such as micelles ("monolayer" spheres), bilayers, or vesicles. Studies of lipid bilayers are very important for our understanding of cell membranes, their behavior and functionality.



a b c

Fig. 1. Molecules used in MD simulations of PNA at lipid bilayer: phospholipid DPPC (a), PNA composed of six bases: GCTAGC (b), and water (c). Different colors represent different atoms: white – hydrogen, grey – carbon, red – oxygen, blue – nitrogen, yellow – phosphor.

Another important bio-molecule is peptide nucleic acids (PNA). PNA is a lab-created analogue of DNA, in which the nucleic bases (adenine, guanine, thymine and cytosine) are attached to a pseudo-peptide backbone. PNA can hybridize to its complementary DNA target in a sequence dependent manner. Unlike most of oligonucleotides analogues, PNA binds very tightly to double-stranded DNA as well. Because of this property PNA molecules are intensively exploited in gene chemistry – a novel, straightforward, and versatile approach for permanently attaching proteins, peptides, fluorophores, and other molecules to plasmid DNA without interfering with transcriptional activity. PNA molecules also have both polar and nonpolar parts – they are still hydrophobic but to some degree soluble in water. In a system containing water, lipid clusters, and PNA molecules, the PNA molecules spontaneously gather at the lipid–water interface due to their limited solubility.

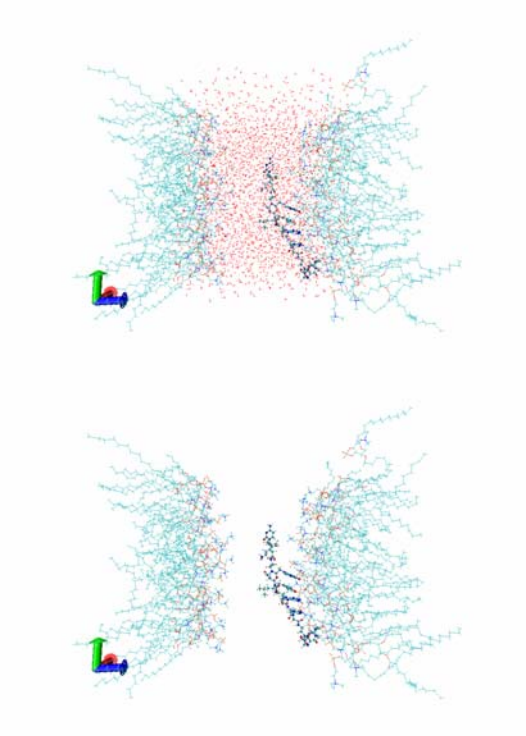


Fig. 2. PNA molecule in water between two lipid layers. Picture (a - top) presents whole the system at equilibrium as simulated using periodic boundary conditions. In picture (b - bottom) water molecules are invisible to make it more readable. Note that the PNA molecule is attached to one of the water – lipid interfaces.

Recently, a new potential application of PNA emerged in a minimal self-replicating nanomachine or protocell design presented by Rasmussen and Chen [1]. According to this design, a minimal protocell able to utilize resources, grow, self-replicate and evolve could be as simple as a small lipid aggregate (micelle) acting as a container by anchoring a PNA molecule to its exterior. In such a protocell, light-driven metabolic processes from the lipid aggregate interior could synthesize lipids and

PNA, with PNA acting as both an information carrier and as a catalyst, leading to a spontaneous growth of the protocell. Micellar lipid clusters in water are thermodynamically stable below some critical size only; therefore the growing protocells would divide as soon as they become large enough, providing the next generation of the protocells.

Research of the simple self-reproducing nanosystems, including theory and experiment, will not only create the basis for a revolutionary and powerful technology with multiple applications, but also provide new insights about the origins of life on Earth. Molecular dynamics (MD) computer simulation is a powerful and suitable method for modeling the phenomena on the molecular level. This approach considers the molecular system's time evolution by considering forces (electrostatic, dispersion, and chemical bonds) acting on individual atoms and numerically solving Newton's equations of motion over short time steps. The time step must be chosen small enough so that constant values of the forces can be assumed to avoid discretization errors. Force parameters used in MD simulations are usually obtained from *ab initio* quantum chemistry computations. Then, the parameters are adjusted usually to ensure reasonable thermodynamics in agreement with experimental data. In our studies we exploit two freeware software packages designed for MD simulation and visualization: NAMD [2] and VMD [3]. Fig. 1 presents the specific molecules, which we study in our MD simulations. Whole the simulated system is shown in Fig. 2.

Acknowledgements

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References

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